WHITE PAPER

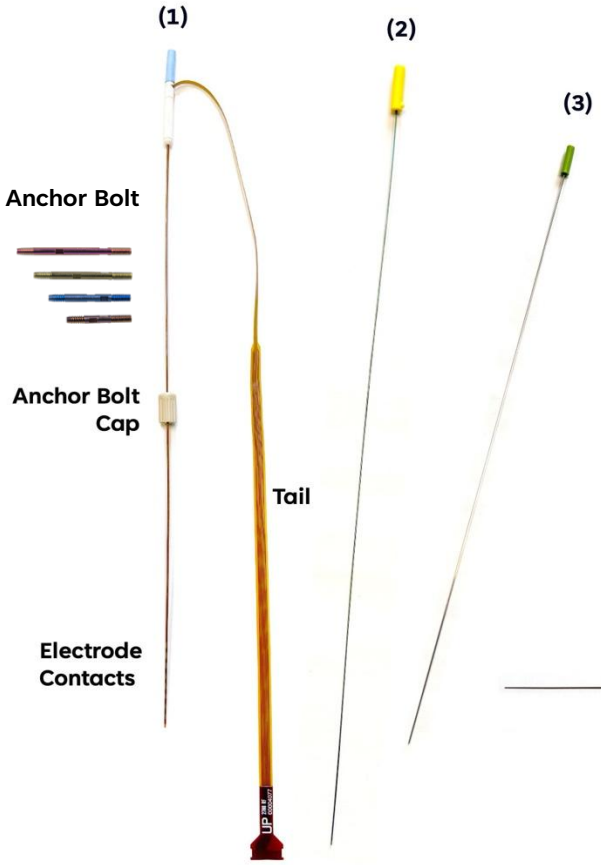
NeuroOne

StereoCED™ — A Scalable Platform *for* CNS Drug Delivery

Authors:
Maria Porto Cruz, Ph.D.,
Parag Patil, M.D., Ph.D.,
David Wambeke,
Aura Kullmann, Ph.D.

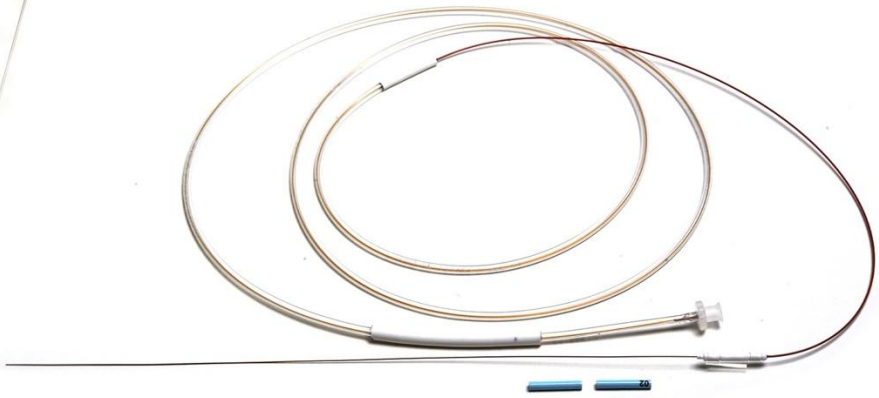
The StereoCED™ Platform*

sEEG-DD Electrode



Drug Delivery Catheter

(Inserted into sEEG-DD Electrode)



SPECS

sEEG-DD Electrode

Electrode used for recording, monitoring and stimulation; Designed to be implanted for a period of less than 30 days

Outer Diameter: 0.8 mm
Number of Contacts: 5 to 16
Contact Size: 2 mm
Materials: Polyimide **/** Platinum

(1 and 3) Implantation / Clearing Stylet

Provides stiffness for placement accuracy during implantation; Clears the lumen of any occlusion accumulated during monitoring period right before delivery

(2) Sealing Stylet

Seals the lumen of the sEEG-DD Electrode during monitoring period

Drug Delivery Catheter

Tubing advanced through the sEEG-DD Electrode lumen to access the delivery site; Designed to be inserted for limited exposure (less than 24 hours) at the time of delivery

Inner Diameter: 0.25 mm
Total Length: 14 ft
Dead Volume: ~ 300 µL
Materials (drug-contacting): PTFE / Fused silica
Connector Type: Standard Luer-Lock

*Device and tools are under development and not approved/cleared by FDA or any Regulatory Agency for sale.

Executive Summary

The human brain is protected by one of the body's most selective defenses: the blood-brain barrier (BBB). This network of tightly joined cells allows oxygen and nutrients to enter the brain while preventing toxins, pathogens, and nearly all large molecules circulating in the bloodstream from getting in.[1]

That same defense presents one of the greatest challenges in delivering therapeutics to the brain. Drugs delivered orally, subcutaneously, or intravenously are largely blocked by the BBB—and the challenge becomes even greater as therapies become larger in size and more complex. Cell and gene therapies, among the fastest-growing areas of pharmaceutical development, are also among the least capable of crossing the BBB.[2]

One way to bypass the BBB is to deliver therapy directly into the cerebrospinal fluid (CSF), either through a spinal injection or via an intraventricular reservoir.[3] While these approaches avoid the BBB, they do not reliably deliver high concentrations of drug to the deep, specific regions of the brain where many neurological diseases originate. Instead, the therapeutic disperses broadly throughout the CSF and penetrates only a limited distance into surrounding brain tissue.[4]

For diseases that require precise treatment of a defined region of the brain, convection-enhanced delivery (CED) has emerged as the leading delivery approach. In CED, a catheter is placed directly into the target tissue, and the therapeutic is infused under gentle, continuous positive pressure. Rather than relying on slow passive diffusion, the pressure actively distributes the therapy throughout the surrounding tissue while largely sparing adjacent healthy brain.[5]

Despite its biological advantages, many existing CED platforms remain difficult to scale commercially. These platforms often require specialized capital equipment, proprietary software, dedicated MRI resources, and lengthy infusion procedures. **Reported treatment times for certain CED gene therapies range from eight to twelve hours.**[6,7,8] These requirements can increase procedural cost, limit the number of hospitals capable of performing treatment, and create a significant bottleneck to the commercial adoption of otherwise promising therapies.

> Every hour saved can reduce OR costs by approximately $2,000–3,000 while also freeing valuable MRI capacity, anesthesia resources, and operating room time for additional patient procedures. [9]

The StereoCED™ drug delivery system from NeuroOne Medical Technologies is being developed to remove these barriers. Rather than requiring specialized infrastructure, StereoCED™ is being designed to integrate with the neurosurgical tools, workflows, and robotic guidance systems already installed in operating rooms worldwide. The system is designed to support both MRI-guided and non-MRI-guided procedures, enables simultaneous multi-catheter infusion, and has the potential to

dramatically reduce procedure times. The result is a delivery platform developed not only for precise therapeutic distribution, but also for the scalable commercial deployment of next-generation brain therapies.

As brain therapeutics continue to advance, targeted drug delivery may increasingly become a limiting factor. The companies that solve the delivery challenge may ultimately create as much value as the companies developing the therapies themselves.

Robotic-Assisted Neurosurgery

Over the past two decades, stereotactic neurosurgery has undergone a fundamental transformation. Procedures that once relied on rigid head frames, painstaking manual coordinate setting, and lengthy operating times are now routinely performed with robotic guidance. Today, the surgeon plans a trajectory using preoperative CT or MRI imaging, and the robot precisely positions instruments along that path. What began as a specialized technology has become the standard workflow at many leading neurosurgical centers. Robotic platforms such as ExcelsiusGPS, ROSA, and NeuroMate are now established fixtures in modern operating rooms, and their installed base continues to expand.

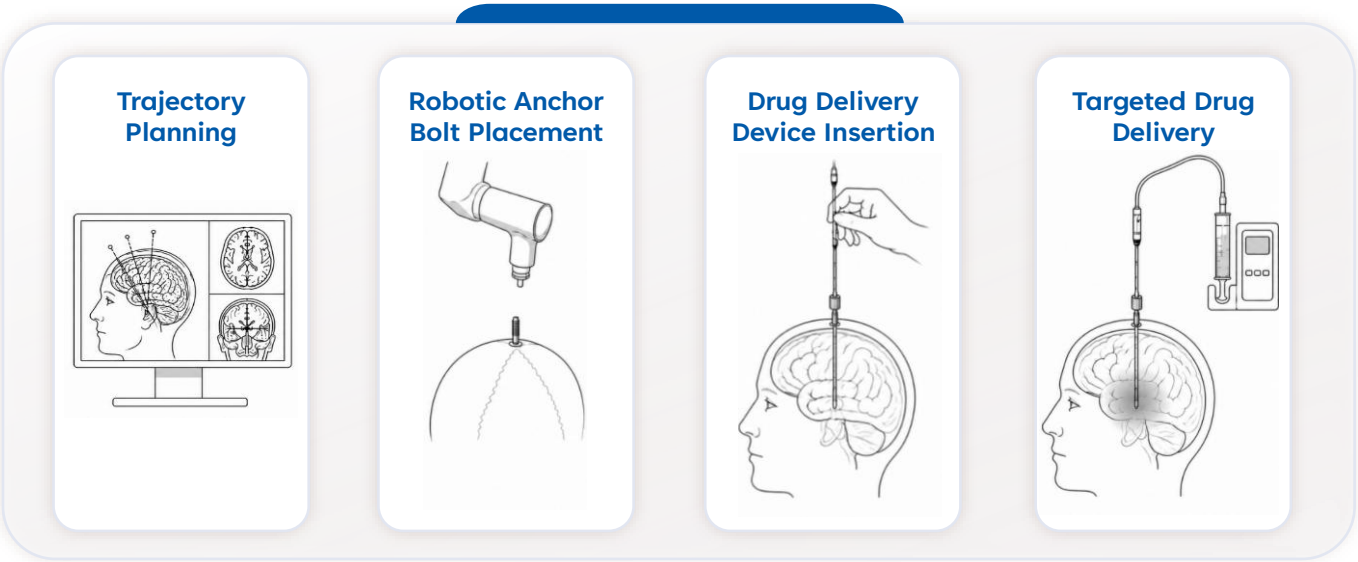
ROSA ONE® Brain
Zimmer Biomet

This robotic workflow now underpins many of the most common stereotactic neurosurgical procedures. Robotic guidance is routinely used for deep brain stimulation (DBS), stereo-electroencephalography (sEEG), stereotactic biopsy, laser interstitial thermal therapy (LITT), and responsive neurostimulation. Although these procedures treat different diseases, they all rely on the same fundamental capability: accurately and reproducibly guiding a linear probe through the brain to a predetermined target while minimizing injury to surrounding tissue.

The StereoCED™ Drug Delivery Platform was adapted from NeuroOne's FDA 510(k)-cleared sEEG electrode technology, for which thousands of devices have been implanted clinically for less than 30 days. As a result, StereoCED™ is being designed to fit naturally within the robotic stereotactic workflows that neurosurgical teams already execute every day. The system is compatible with both traditional frame-based stereotaxy and modern robotic guidance, allowing hospitals to leverage

existing capital equipment, trajectory-planning software, and surgical techniques. Rather than asking hospitals to adopt an entirely new procedural workflow, StereoCED™ extends an established robotic targeting ecosystem to brain drug delivery—positioning next-generation therapeutics to benefit from the speed, precision, and scalability that robotic stereotactic surgery has already brought to modern neurosurgery.

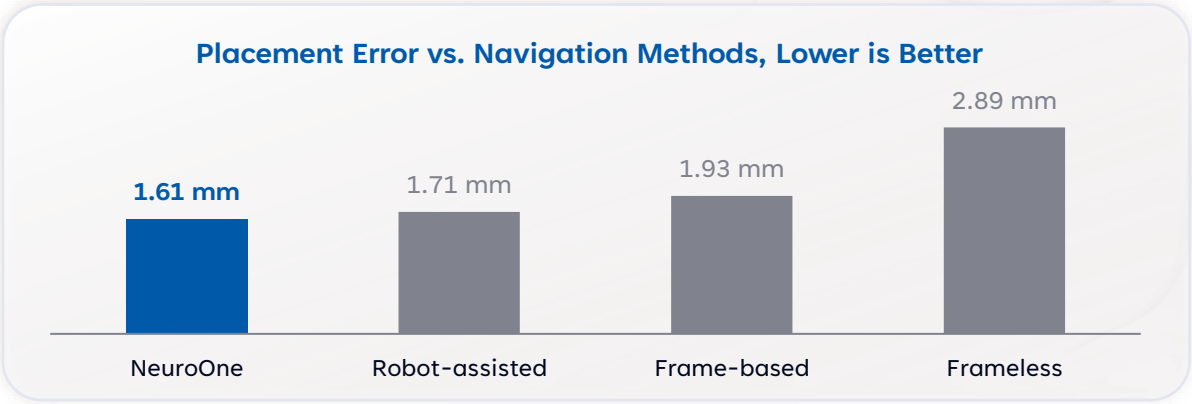
Illustrative StereoCED™ Robotic-Assisted Drug Delivery Workflow



Accuracy and Ultra-thin Profile

Accuracy. In intraparenchymal delivery, the drug distribution begins where the cannula/catheter tip lands. A trajectory that drifts significantly can seed the drug cloud in the wrong place — off the target, into a ventricle or CSF space, or too close to a vessel. Accurate placement is the foundation everything else is built on.

StereoCED™ is built on NeuroOne's sEEG platform, and that platform's placement accuracy is well characterized. In a robot-assisted (ROSA) and CT-guided cadaveric study of 24 implants, the sEEG electrode delivered 1.28 mm mean entry-point error and 1.61 mm mean target-point error, with zero user errors across all placements — ahead of both frame-based and frameless navigation and in line with the best robot-assisted benchmarks.[9] And it is accuracy in the right context: because CED deposits a centimeter-scale drug cloud rather than making point contact, a ~1.6 mm offset is a clinically insignificant fraction of the infusion footprint.



Ultra-thin profile. The StereoCED™ device outer diameter is a mere 0.8 mm in diameter. Certain CED devices are two or even three times thicker — and outer diameter is not a cosmetic detail. A larger diameter device displaces and injures more brain tissue along its trajectory, raises the risk of hemorrhage, and opens a larger channel into which infusate can reflux (backflow).[10,11,12] A thinner device does the opposite: less trauma, lower reflux potential, and a footprint small enough that placing many trajectories becomes practical rather than punishing. Being minimally invasive at each site is part of what makes multi-trajectory delivery viable at scale.

Multi-Trajectory, Simultaneous Infusion Sites

Some of today's leading CED procedures place two trajectories at a time — one in each hemisphere. A frame is mounted over a burr hole on each side, a cannula is advanced along a planned trajectory into the target, and therapy is infused slowly while the cannula is stepped along its trajectory to extend the therapeutic distribution. For some indications, a single bilateral placement of this kind is enough.

For others, it is only the beginning. Covering a large or irregular structure can require several trajectories per side, and because only one pair is placed at once, the cannulas must be removed, repositioned, and re-infused in successive rounds until the target is filled. Each round adds another pair of placements, another slow infusion, and another block of time on the operating day. For some therapies, the full procedure can stretch across the better part of the entire day.

The StereoCED™ Drug Delivery System takes a fundamentally different approach: multiple trajectories, infused simultaneously. StereoCED™ is built on NeuroOne's sEEG platform, which routinely places more than ten trajectories in a single procedure.[13]

The advantages of a multi-trajectory, simultaneous infusion approach are substantial.

Speed. When trajectories are placed only a pair at a time, procedure time is additive — each round of placement and infusion is added to the last, and a complex target consumes hours. Simultaneous infusion collapses that sequence: many catheters deliver in parallel, so total infusion time is governed

by a single infusion rather than the sum of many. Hours may come out of the procedure, freeing operating room capacity, reducing anesthesia exposure, and increasing the number of patients a center can treat.

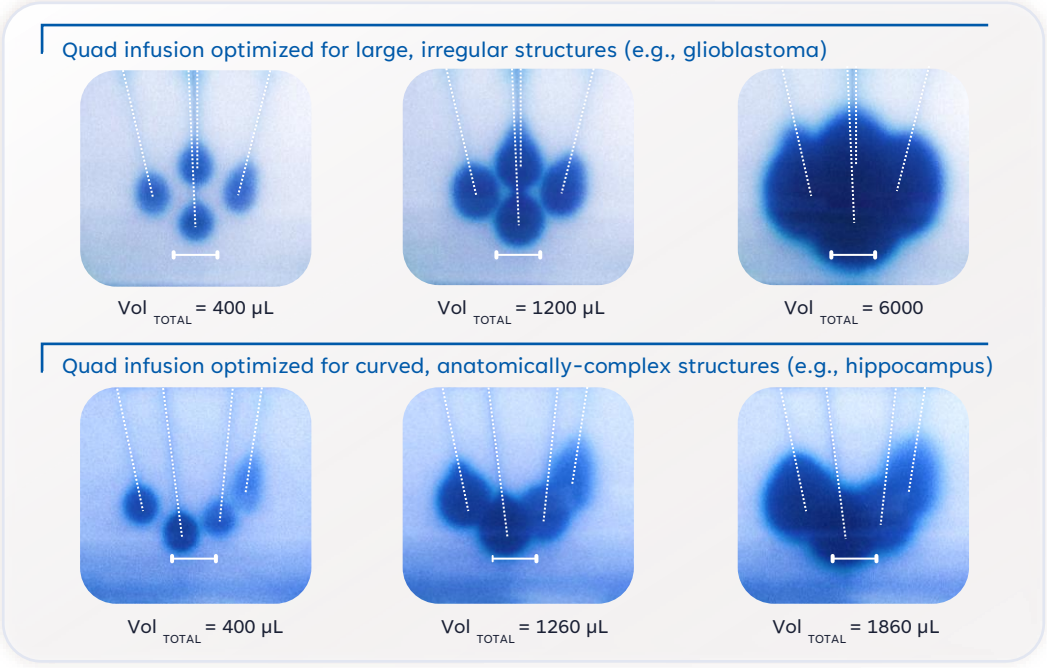
Reduced reflux and greater reproducibility. Covering a large volume from a single trajectory demands a large infusion — and large infusions require higher flow rates and pressures. Elevated infusion pressure is a primary driver of reflux, in which drug tracks backward along the catheter instead of distributing into the targeted tissue[14]. Dividing the same total volume across multiple catheters keeps each individual infusion smaller and at a lower pressure. The result is potential for less reflux, less variability, and a distribution that is more predictable and more reproducible from one procedure to the next.

Coverage of irregular anatomy. Many of the most important targets in the brain are neither small nor spherical. The striatum, the target of gene therapy for Huntington's disease, is a large subcortical structure with a complex three-dimensional shape; the epileptogenic hippocampus is elongated and C-shaped; the infiltrative margin of a glioblastoma is irregular and wraps the resection cavity. A single expanding infusion may not conform to shapes like these. Multiple, independently planned trajectories, each covering a defined region, can tile together to match the true anatomy of the disease. Each catheter is independently controllable, enabling individualized infusion volumes and infusion durations for each trajectory.

Speed, reproducibility, and conformance to the anatomical target are the three requirements for delivering complex brain therapies at scale — and all three are performance goals built into StereoCED™ from the start.

Concept of Multi-trajectory Demonstrated in a Benchtop Model

(agarose gel and methylene blue dye) · Quad infusion = four simultaneous infusion sites, Scale bar = 1 cm



MRI Optionality

The StereoCED™ drug delivery system is being designed to support *both* MRI-guided and non-MRI-guided procedures, giving users critical optionality.

MRI compatibility is a valuable tool during research and early clinical development. Real-time imaging allows the infusion to be visualized as it happens, confirming target coverage while the drug is being delivered.[15] A contrast tracer such as gadolinium is routinely co-infused with the therapeutic; because the tracer disperses with the drug, its spread on MRI serves as a real-time surrogate for where the therapeutic is going. During the phases when a delivery approach must be validated and a distribution profile established, that visual confirmation is clinically significant.

But real-time MRI guidance is not free. Performing an infusion inside the scanner consumes hours of one of the hospital's most expensive and capacity-constrained resources. Every hour dedicated to a drug delivery procedure is an hour the MRI cannot be used for diagnostic imaging or other reimbursable studies, creating substantial opportunity costs. Unlike MRI, CT scanners are generally more accessible, less expensive to acquire and operate, and capable of completing imaging studies in less time.[16,17] As a result, CT capacity is typically easier to access and far less disruptive to hospital operations. As these therapies move from a handful of research centers toward broad clinical adoption, dedicating an MRI suite to a multi-hour infusion shifts from an enabling technology to a practical bottleneck.

The vast majority of NeuroOne's sEEG electrodes are placed robotically under CT guidance, and drug delivery is the same. Patients typically undergo a short pre-operative MRI, which is then fused with the intraoperative CT for trajectory planning.

This is where MRI optionality becomes strategically important. Rather than occupying an MRI suite throughout the infusion, a procedure could instead be planned using a conventional preoperative MRI, the delivery catheters placed stereotactically with a brief CT-guided procedure, and the therapeutic infused without continuous imaging. That workflow is only possible if clinicians have confidence that the drug will distribute as intended without needing to watch it unfold in real time.

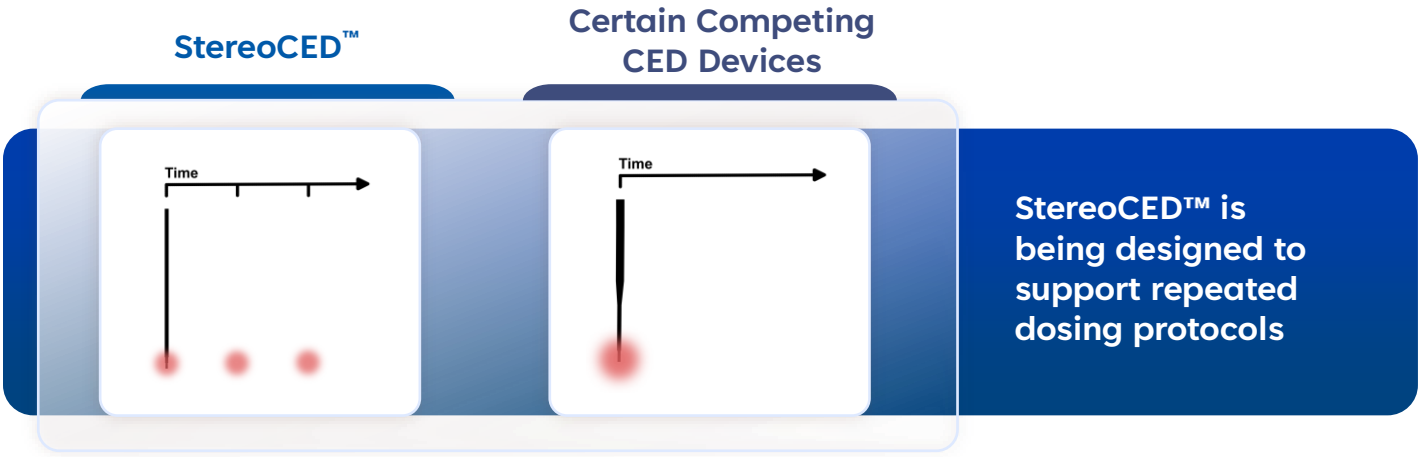
StereoCED™ is being designed with that objective in mind, and the majority of NeuroOne's sEEG electrodes are already implanted robotically under CT guidance in routine clinical practice. StereoCED™ builds on that proven workflow with a multi-trajectory architecture designed to promote more consistent drug distribution through multiple simultaneous, lower-pressure infusions. If that consistency can be achieved, MRI becomes a tool used when it provides unique value—in research, early clinical development, or particularly complex cases—rather than a requirement for every procedure.

StereoCED™ Platform Performance Objectives

Repeat Dosing

Certain CED systems are designed for a single procedure and not intended for long-term implantation[18]. Once the infusion is complete, the catheter is removed and subsequent treatments require a new surgical intervention. While this approach is appropriate for one-time therapies—including many gene and cell therapies—a growing number of CNS applications may benefit from repeat dosing. Glioblastoma is a compelling example, where recurrent disease may require multiple administrations of therapeutic agents over time rather than a single treatment.

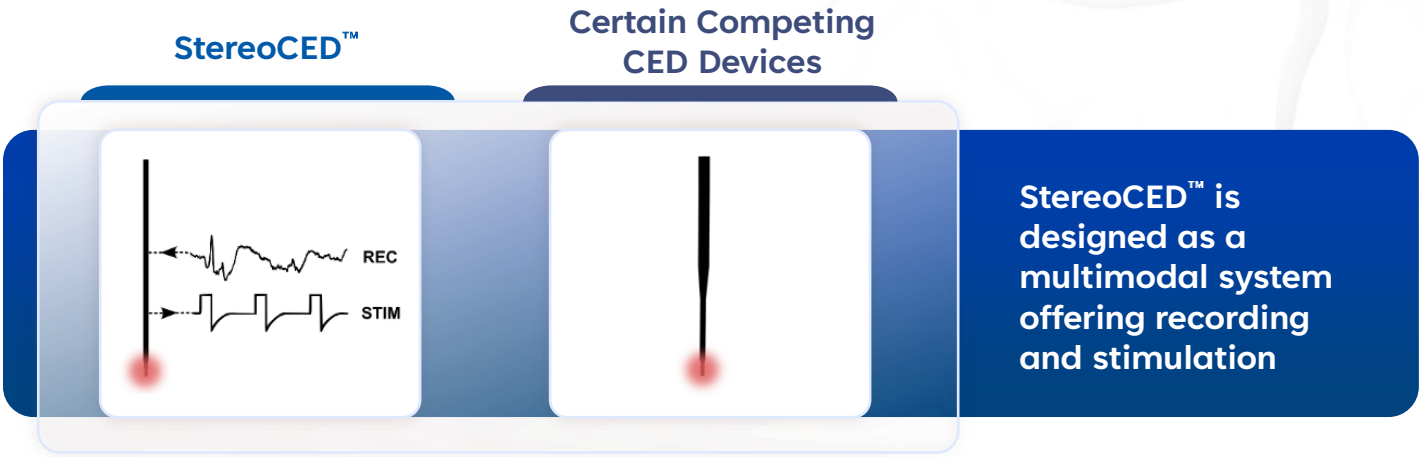
The StereoCED™ drug delivery device is being developed for implantation for less than 30 days, leveraging NeuroOne's existing FDA-cleared sEEG technology, where intracranial electrodes routinely remain implanted for extended neurological monitoring. This capability has the potential to transform drug delivery from a one-time intervention into a treatment platform capable of delivering therapy on the schedule dictated by the disease rather than by the limitations of the device.



Integrated Electrophysiology

Because StereoCED™ is built upon NeuroOne's proven sEEG platform, the same implanted device used to deliver therapy is also designed to record intracranial electrophysiological activity. This creates the potential for simultaneous therapy delivery and functional monitoring through a single implant.

For disorders such as epilepsy, electrophysiological activity may provide a more immediate and sensitive measure of therapeutic response. Recording directly from the treated tissue could provide valuable insights into treatment effect, enable longitudinal monitoring, and ultimately support the development of closed-loop or adaptive therapeutic strategies.



Adjustable Catheter Geometry

The geometry of a CED cannula/catheter plays an important role in drug distribution. Fixed stepped-tip design predetermines the geometry and cannot be optimized for different therapeutic targets or infusion strategies.

StereoCED™ incorporates an adjustable distal step, which is designed to allow the operator to modify the final catheter geometry based on the intended application. This introduces an additional degree of control over drug distribution, enabling optimization of the infusion profile for different anatomical targets, therapeutic agents, or treatment objectives. Combined with NeuroOne's multi-trajectory architecture, this design offers the potential to further improve spatial coverage while tailoring drug delivery to the unique characteristics of each procedure.

Summary

The field of brain-delivered therapeutics is moving beyond the clinic and into the commercial setting—and that transition is illuminating the potential shortcomings of current CED approaches. Techniques that were acceptable when a few trial centers treated a few patients may become bottlenecks at scale: dedicated MRI suites, specialized capital equipment, and infusions that consume the better part of a surgical day.

StereoCED™ is being designed to overcome these barriers and enable scalable, commercially viable intracranial drug delivery. Rather than requiring hospitals to adopt new infrastructure, it extends the robotic stereotactic workflow already established in operating rooms worldwide. Built upon NeuroOne's FDA-cleared sEEG platform, StereoCED™ combines well-characterized placement accuracy with an ultra-thin device profile, simultaneous multi-trajectory infusion, and MRI optionality. Together, these design features have the potential to shorten procedures, reduce reliance on dedicated MRI resources, improve coverage of complex anatomy, and support more reproducible drug delivery.

The implications extend beyond any single therapy. Repeat dosing through an implanted device, integrated electrophysiological recordings, and adjustable catheter geometry position StereoCED™ as a delivery platform rather than a single-use tool—one designed to support gene therapies, cell therapies, oncology programs, and future CNS therapeutics across multiple partners. As brain therapeutics continue to mature, the platforms that make delivery scalable, reproducible, and broadly accessible may ultimately capture as much value as the therapies they enable.

Approval is won on the molecule; adoption is won on delivery.

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